REMARKS

The Present Invention

The present invention pertains to isolated or purified nucleic acid molecules, host cells or organisms, pharmaceutical compositions, a method for diagnosing cancer in a mammal, methods of detecting cancer or a predisposition to cancer in a mammal, and a method of preparing a pharmaceutical composition.

The Pending Claims

Claims 1-4, 30, 31, 35-66 are pending, of which claims 1-4, 30, 31, 37, 39, 49-52, 64, and 65 and are directed to pharmaceutical compositions, claims 35, 38, 40-43 are directed to an isolated or purified nucleic acid molecule, claims 36 and 44-48 are directed to host cells or non-human organisms, claims 53-55 are directed to a method of detecting cancer in a mammal, claims 56-58 are directed to a method of detecting a predisposition to cancer, claims 59-63 are directed to a method of detecting cancer or predisposition to cancer in a mammal, and claim 66 is directed to a method of preparing a pharmaceutical composition.

The Amendments to the Claims

Claims 6-16, 29, and 32-34 have been cancelled. Applicants reserve the right to pursue any cancelled subject matter in a continuation, continuation-in-part, divisional, or other application. Cancellation of any subject matter should not be construed as abandonment of that subject matter.

Claims 1-4, 30, 31, 37, and 39 have been amended to be directed to a pharmaceutical composition that is suitable for administration to a human. Pharmaceutical compositions suitable for administration to a human are supported by the specification at, for instance, page 72, line 11, and original claim 23. Claims 1, 4, 30, 37, and 39 have been further amended to recite "and a pharmaceutically acceptable carrier" which recitation is implicitly supported in the instant application. Specifically, one of ordinary skill would have recognized that pharmaceutical compositions ordinarily comprise a pharmaceutically acceptable carrier. In this regard, no new matter has been added by way of this amendment.

Claims 1 and 30 have been further amended to recite "comprising" in lieu of "consisting of." Claim 35 has been amended to recite "inhibits tumor cell growth" instead of "possesses tumor growth inhibiting activity, focus formation inhibiting activity, and an ability to bind to Raf-1." Also, claim 35 has been amended to delete "wherein the derivative comprises an amino acid substitution in SEQ ID NO: 5" and instead recite "wherein the

isolated or purified nucleic acid has at least 30% identity with SEQ ID NO: 5", which is supported by the specification at, for instance, page 13, lines 8-11 and lines 19-22. Claim 36 has been amended to recite "or non-human organism," which is supported in the specification at, for instance, page 32, lines 16-22. Claims 37 and 39 have been amended to recite "wherein the nucleic acid optionally is in a cell" which is supported by the specification at, for instance, page 32, lines 16-22, and page 39, line 26, through page 40, line 5.

Claims 40-66 have been added. Support for claim 40 is found in the specification at, for instance, page 20, lines 21-27. Claim 41 is supported by the specification at, for instance, page 21, lines 2-7. Claims 42 and 43 are supported by the specification at, for instance, page 25, line 25, through page 13, line 5. Claims 44-48 are supported by the specification at, for example, page 32, lines 16-22, and page 39, line 26, through page 40, line 5. Claims 49-52 are supported by the specification at, for instance, page 72, lines 11-18, and original claim 23. Claims 53-58 are supported by the specification at, for instance, original claim 6, page 65, line 20, through page 67, line 24, page 72, lines 19-26, and page 39, lines 3-25. Claims 59-63 are supported by the specification at, for example, page 46, line 19, through page 26, line 29. Claims 64 and 65 are supported by the specification at, for example, page 72, lines 11-18 and original claim 23. Claim 66 is implicitly supported by the specification. Specifically, one of ordinary skill would have recognized that pharmaceutical compositions ordinarily comprise a pharmaceutically acceptable carrier, such that a method of preparing any pharmaceutical composition comprises combining the pharmaceutically active ingredient with a pharmaceutically acceptable carrier, diluent, or excipient.

Accordingly, no new matter has been added by way of these amendments.

Interview Summary

Applicants wish to thank Examiner Schnizer for the courtesies extended to applicants' representatives David Schodin and Julie Hong during the telephonic interview held on August 30, 2004. In the interview, the prior art rejection was discussed as it pertains to the recombinant expression vector claims. Since the prior art, especially, Lamerdin et al., fails to teach or suggest the tumor suppressing activity of Rig, it was proposed to amend the claims essentially as set forth in this Amendment. Examiner Schnizer considered whether the proposed pharmaceutical compositions might have been obvious because any recombinant expression vector comprising the Rig gene and a standard laboratory buffer could be construed as a pharmaceutical composition. While no agreement was reached, Examiner Schnizer agreed to fully consider the claims discussed, if submitted via an Amendment.

Discussion of the Rejection under 35 U.S.C. Section 112, second paragraph

The Office Action rejects claims 32 and 34-39 under 35 U.S.C. Section 112, second paragraph, as allegedly indefinite. This rejection is traversed for the reasons set forth below.

The Office Action rejects claims 32, 34, 37, and 39 for reciting only a single component of the claimed composition. Claims 32 and 34 have been cancelled. Claims 37 and 39 as amended recite "pharmaceutical compositions." Thus, the rejection as it pertains to these claims is believed to be moot. In view of the foregoing amendments, the rejection on this ground is moot.

Claims 35-39 are rejected for the recitation of "derivative." This term has been removed from claim 35, therefore, the rejection on this ground is moot.

The Office rejects claims 35-39 for the recitation of "substantially homologous." Specifically, the Office Action states that the specification fails to identify the lower limit on the degree of identity necessary to qualify as "substantially homologous." In the context of the present application, however, the term "substantially homologous" is not indefinite. The specification defines this term as a partially complementary sequence [...] that at least partially inhibits a completely complementary sequence from hybridizing to a target nucleic acid (page 13, lines 8-11). The specification also identifies a lower limit on the identity that a substantially homologous sequence must have by defining a sequence which lacks a partial degree of complementarity. The latter is defined as one with less than about 30% identity (page 13, lines 19-22). In this regard, the term "substantially homologous" (and, therefore, claims 35-39) is clear.

In view of the foregoing, the pending claims are clear and definite. Therefore, Applicants respectfully request that the rejection under Section 112, second paragraph, be withdrawn.

Discussion of the New Matter Rejection

The Office Action rejects claims 1-4 and 35-39 under Section 112, first paragraph, as allegedly lacking written description and as allegedly containing new matter. These rejections are moot in view of the claim amendments.

Claims 1-4 are rejected, since the specification allegedly does not provide written support for any vector consisting of only regulatory sequences operably linked to a nucleic acid sequence encoding SEQ ID NO: 5. However, the claims no longer recite "a recombinant expression vector consisting of an open reading frame operably linked to one or more regulatory elements."

Claims 35-39 are rejected for allegedly not limiting the number of amino acid substitutions that may be made in SEQ ID NO: 5, nor specifying the nature of the tumors or foci that may be inhibited. Claim 35 has been amended so as to remove the recitations of "amino acid substitution in SEQ ID NO: 5" and "possesses tumor growth inhibiting activity, focus formation inhibiting activity, and an ability to bind to Raf-1." Thus, the rejection as it applies to these claims is moot.

It is noted that claim 35 continues to recite "inhibits tumor cell growth." However, Section 112, first paragraph, does not require the claim to recite which tumor cells are inhibited.

In view of the foregoing, Applicants submit that the rejection under Section 112, first paragraph, should be withdrawn.

Discussion of the Written Description Rejection

The Office Action rejects claims 35-39 under Section 112, first paragraph, as allegedly lacking written description. This rejection is moot in view of the claim amendments, or should otherwise be withdrawn.

Claims 35-39 allegedly did not have any structural limitations pertaining to the claimed nucleic acid molecules. Claim 35, however, requires that the nucleic acid molecule is substantially homologous, which means that the molecule must have at least 30% identity to SEQ ID NO: 5 and must at least partially inhibit the hybridization of SEQ ID NO: 5 from its complementary sequence.

The Office Action further states that the specification fails to disclose a single variant of SEQ ID NO: 5 as claimed. Accordingly, it appears that the Office is relying on the disclosure of a nucleotide sequence of such a variant to meet the written description requirement. However, as noted in the Office's Guidelines for Written Description Requirement, published in the Federal Register, Volume 66, No. 4, page 1101, Response to Comment 9 (January 5, 2001) (copy attached hereto), there is no basis for a *per se* rule requiring disclosure of complete DNA sequences when claiming DNA sequences. In the present case, such description is not required because the mere mention of variants in the specification in conjunction with the disclosure of a nucleotide sequence is a *de facto* disclosure to one of ordinary skill in the art of many such sequences.

The Office Action also alleges that the specification fails to disclose any relevant identifying characteristic such as any correlation between any polypeptide and any of the required functions. Applicants request clarification or withdrawal of the rejection because the Examiner has clearly comprehended that SEQ ID NO: 5 and variants thereof have the

required functions. Applicants also have shown that a S21N mutation of the Rig amino acid sequence (SEQ ID NO: 5) prevents the protein from inhibiting Ras-mediated transformation and formation of foci. Accordingly, Applicants disclose that SEQ ID NO: 5 has the claimed properties and that the serine at position 21 is important for the tumor growth inhibiting function of Rig. Furthermore, Applicants have demonstrated that the ability to bind GTP is crucial for the Rig protein to function as a tumor suppressor.

In view of the foregoing, the claims are adequately described.

Discussion of the Enablement Rejection

The Office Action rejects claims 35-39 under Section 112, first paragraph, as allegedly lacking enablement. Specifically, the specification allegedly fails to teach what are the minimum sequence and functional characteristics a given polypeptide must have in order to perform the functions recited in claim 35. This rejection is traversed for the reasons set forth below.

Claims 35-39 are rejected for allegedly not having any structural limitations pertaining to the claimed nucleic acid molecules. As discussed above, claim 35 requires that the nucleic acid molecule is substantially homologous, which means that the molecule must have at least 30% identity to SEQ ID NO: 5 and must at least partially inhibit the hybridization of SEQ ID NO: 5 from its complementary sequence. Accordingly, claim 35 does, in fact, recite a structural limitation.

Furthermore, as regards the minimum sequence that the protein must have in order to inhibit tumor cell growth, Applicants have shown that a S21N mutation of the Rig amino acid sequence (SEQ ID NO: 5) prevents the protein from inhibiting Ras-mediated transformation and formation of foci. Accordingly, Applicants disclose that the serine at position 21 is important for the tumor growth inhibiting function of Rig.

In view of the foregoing, Applicants assert that the claimed invention is enabled by one ordinarily skilled in the art. Therefore, Applicants request that the lack of enablement rejection be withdrawn.

Discussion of the Rejections under 35 U.S.C. Section 103 (a)

The Office Action rejects claims 6-11, 13-15, and 29 under Section 103 (a) as allegedly obvious in light of Lamerdin et al. (GenBank Accession No. AC006538), and Kimmelman et al. (*Oncogene* 15(22): 2675-2685 (1997)). The Office Action also rejects claim 12 under Section 103 (a) as allegedly obvious in view of Lamerdin et al., Kimmelman et al., Mullis et al. (U.S. Patent 4,965,188), and Takarada (U.S. Patent 5,981,183). Claim 15

is further rejected under Section 103 (a) as allegedly obvious in view of Lamerdin et al., Kimmelman et al., and Mullis et al. The Office Action rejects claim 16 under Section 103 (a) as allegedly obvious in view of Lamerdin et al., Kimmelman et al., Erlich et al. (U.S. Patent 5,314,809), and DeBoer et al. (U.S. Patent 5,392,703). The Office Action rejects claims 30-34 under Section 103 (a) as allegedly obvious in view of Lamerdin et al., Kimmelman et al., and the 1997/1998 Stratagene catalog. Reconsideration of these rejections is requested for the reasons set forth below.

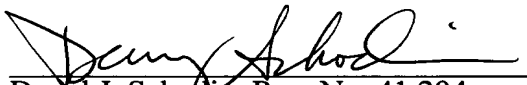
All of the rejected claims, except for claims 30 and 31, have been cancelled. The rejection, therefore, is moot as it pertains to the cancelled claims. Claims 30 and 31 have been amended to be directed to pharmaceutical compositions that are suitable for administration to a human. None of the above references, either alone or in combination, teach or reasonably suggest the pharmaceutical compositions suitable for administration to a human. Prior to the filing of the instant application, there was no appreciation that the Rig protein is a tumor suppressor protein, which is useful in the treatment of cancer. Accordingly, one of ordinary skill in the art would not have been motivated to make a pharmaceutical composition suitable for administration to a human comprising the Rig gene. Even if a laboratory was practicing GLP when experimenting with a recombinant expression vector comprising the Rig gene, it does not necessarily follow that the resulting composition constituted a pharmaceutical composition suitable for administration to a human. An invention is not inherently anticipated by the prior art unless practice of the prior art would always and inevitably lead to the claimed invention. In view of the foregoing, the pharmaceutical compositions as claimed herein are neither inherently anticipated nor obvious. Therefore, Applicants request that the rejection under Section 103 (a) be withdrawn.

New claim 65 also requires that the pharmaceutical composition, which is suitable for administration to a human, is made under cGMP. The composition comprises a recombinant expression vector comprising the Rig gene. Nothing in the prior art of record teaches or reasonably suggests a Rig expressing pharmaceutical composition made under cGMP. Moreover, not all laboratories practice cGMP. cGMP is ordinarily carried out when conducting experimental studies that support or are intended to directly support applications for research or marketing permits for products regulated by the U.S. Food and Drug Administration. Therefore, it cannot be assumed that *any* laboratory experimenting with the Rig gene in an expression vector practices cGMP.

Conclusion

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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